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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/508,527 | 07/17/2000 | AKIKO ITAI | P19291 | 1282 |

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| EXAMINER | |
|---|---|
| KIM, YOUNG J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 06/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/508,527 | ITAI, AKIKO | |
| | Examiner | Art Unit | |
| | Young J. Kim | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 3-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 14, 2005 has been entered.

### *Preliminary Remark*

Claims 1 and 3-10 are pending and are under prosecution.

### *Claim Rejections - 35 USC § 112*

The rejection of claims 1 and 3-10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on October 14, 2004 is withdrawn in view of the Amendment received on April 14, 2005.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because there appears to be a disconnect between the method regarding the "conducting" step and the "choosing" step. The conducting step is recited as

conducting matching based on the *environmental information on each amino acid residue of each of the two or more core segment sequences of the reference protein* and hydrophobicity or hydrophilicity property of the side chain of each amino acid residue of the query sequence. This step is construed as comparing/matching the environmental information of a segment of amino acid residue of the reference protein to that of the query protein. However, the "choosing" step is recited as choosing at least one template protein among the reference protein that has highest similarity in *three-dimensional structure to the protein* comprising the query sequence. Hence, this step is solely based on the similarity of the three-dimensional structure of the reference proteins and the query protein. There is a clear disconnect between how the reference proteins identified in the "conducting" step is related to the "choosing" step.

For the purpose of compact prosecution, it is assumed that the reference proteins employed in the "choosing" of at least one template protein are reference proteins that are generated from the "conducting" step.

Claims 3-10 are indefinite by way of their dependency on claim 1.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1 and 3-10 under 35 U.S.C. 102(b) as being anticipated by Eisenberg et al. (U.S. Patent No. 5,436,850, issued July 25, 1995), made in the Office Action mailed on October 14, 2004 is maintained for the reasons of record.

Applicants' arguments presented in the Amendment received on April 14, 2005 have been fully considered but they are not found persuasive for the following reasons.

Applicants' arguments are addressed in the same order they were presented.

Applicants refer to the Telephonic Interview dated on September 4, 2003, where the Examiner of record agree to withdraw the rejection under 102(b) based on the Eisenberg reference (Patent No. 5,436,850) if the amendment of introducing "of two or more segment sequences" were made. Applicants contend that as the agreement had been made and since the claims have been amended as agreed upon and as new prior art had not been applied, the re-application of the same rejection would be "misplaced." (page 9, 1st paragraph, Response).

In the above-mentioned interview, Applicants were advised that further search would be necessary in order to determine whether the newly introduced limitation would be patentable over prior art. Applicants also acquiesce this point (page 5, Amendment received on September 10, 2003).

In further search and examination, U.S. Patent No. 6,512,981 B1, the second Eisenberg et al. reference, was discovered, which demonstrated the inherency of the teachings of the Eisenberg et al. reference previously applied.

To expound, the Eisenberg et al. reference cited under 102(b) rejection taught a "dynamic programming," but did not further describe what entails this programming (column 10, lines 61-67), but a specific reference to the preferred

**In particular, all sequences in a database of target sequences are aligned with the 3D structure profile using a dynamic programming algorithm, which allows insertions and deletions in the alignment. Preferred dynamic programming algorithms are taught in S. B. Needleman, C. D. Wunsch, *J. Mol. Biol.*, 48, 443–453 (1970) and T. F. Smith, M. S. Waterman, *Adv. Appl. Math.*, 2, 482–489 (1981), and their use is discussed and**

dynamic programming is disclosed and referred to:

This was clearly communicated in the Office Action mailed (mailed subsequent to the Interview) to the Applicants (page 6, 3rd paragraph, Office Action mailed on October 1, 2003):

> The '850 patent does not explicitly disclose that the comparison of the sequences involve segmentation of the reference protein into two or more segments, wherein the segments comprise two or more continuous amino acid residues.

However, Eisenberg et al. (U.S. Patent No. 6,512,981 B1, issued January 28, 2003, priority May 1, 1997) disclose the ***inherent property*** of dynamic programming algorithm which '850 patent employs:

In the second Eisenberg et al. reference, ('981 patent), the artisans refer to the same "dynamic programming," referring to the same set of references mentioned in the '850 patent, with the difference being in that the reference actually describes what this process does (column 9, lines 29-42).

Alignment Algorithm

In the preferred embodiment of the invention, the optimal alignment between the derived properties of a probe sequence and the structural properties of a target is carried out using a dynamic programming algorithm. Dynamic programming algorithms are taught in Needleman & Wunsch, *J. Mol. Biol.*, 48, 443–453 (1970) and Smith & Waterman, *Adv. Appl. Math.*, 2, 482–489 (1981), and their use is discussed and demonstrated in Gribskov et al., *Proc. Natl. Acad. Sci. U.S.A.*, 84, 4355 (1987); Gribskov et al., *CABIOS* 4, (1988); Gribskov & Eisenberg, in "Techniques in Protein Chemistry" (T. E. Hugli, ed.), p. 108. Academic Press, San Diego, Calif., 1989; Gribskov et al., *Meth. in Enz.* 183, 146 (1990) (all incorporated herein by reference). Any comparable search technique could also be used.

In the description, Eisenberg et al. evidences the inherency of the limitation, "two or more segments." This was clearly communicated to Applicants in the Office Action mailed on October 1, 2003 (reproduced below, page 6 of the Office Action):

> "The "local" algorithm finds the highest-scoring aligned segment, allowing unpenalized-unaligned N- and C-termini both in the sequence and in the structure. The "global" alignment algorithm allows at most two unaligned termini without penalization, but requires that at least one N-terminus segment and one C-terminus segment of either the sequence or the structure be either aligned or penalized. The preferred embodiment uses a different variation, dubbed the "global-local" alignment. This algorithm does not penalize unmatched N- or C-termini segments in the probe sequence (local alignment), but does penalize any gaps in the target structure (global alignment). This variation produces more reliable scores than those obtained by the commonly used global or local

Therefore, the rejection was maintained not only on the basis of the first

Eisenberg et al. reference alone, but was based on the inherency demonstrated by the second Eisenberg et al. reference.

Further search was conducted.

A prior art not cited previously was cited in order to demonstrate inherency.

Therefore, it is unclear why Applicants would contend that the rejection is misplaced.

Applicants' argument is not found persuasive therefore.

Next, Applicants state that in order to expedite prosecution, the claims explicitly state that the matching is based on each amino acid residues of each of the two or more core segment sequences of the reference protein. (page 9, 1st paragraph, bottom, Response).

Examiner notes that the phrase, "two or more segment sequences" had already been present in the finally rejected claims.[1] Thus, it appears that Applicants are contending that the addition of the term, "core" to the phrase renders the claimed invention un-anticipated.

This is not found persuasive because absent a specific definition regarding the term, "core segment," any segment comprising two or more contiguous amino acid residues would necessarily meet the limitation.

In support for the new limitation, Applicants pointed to page 10, second paragraph; and page 19, lines 5 and 6 (page 7, bottom paragraph, Response).

No support was found for the term, "core segment," rendering the claims anticipated by Eisenberg et al.

Next, Applicants contend that the rejection does not point to any teachings in the first Eisenberg et al. reference, instead points to teachings in the second Eisenberg et al. reference,

[1] See Amendment received on June 21, 2004.

"whose provisional application was filed more than two years after the issuance of the first Eisenberg et al. reference, concluding that it was insufficient to establish inherency.

To the contrary, the first Eisenberg et al. reference does discuss the use of "dynamic programming" with respect to their disclosed invention (column 10, lines 61-67):

> **In particular, all sequences in a database of target sequences are aligned with the 3D structure profile using a dynamic programming algorithm, which allows insertions and deletions in the alignment. Preferred dynamic programming algorithms are taught in S. B. Needleman, C. D. Wunsch, *J. Mol. Biol.*, 48, 443–453 (1970) and T. F. Smith, M. S. Waterman, *Adv. Appl. Math.*, 2, 482–489 (1981), and their use is discussed and**

Artisans clearly state, "[i]n particular, all sequences in a database of target sequences are aligned with the 3D structure profile ***using a dynamic programming algorithm***." (emphasis added) The disclosure could not be more clear in stating that dynamic programming is employed in their invention.

With regard to Applicants' arguments drawn to the issue date of the first Eisenberg et al. reference being more than 2 years prior to the second Eisenberg et al. reference, the argument is not found persuasive because the "dynamic programming" referred to by both of the references refer to the same publication, evidencing that the dynamic programming employed by the first Eisenberg et al. reference is that which is described in the second Eisenberg et al. reference.

Applicants' arguments are not found persuasive and the rejection is maintained therefore.

Claims 1, 3-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Cohen et al. (U.S. Patent No. 5,878,373, issued March 2, 1999, filed December 6, 1996).

Cohen et al. disclose a computer-assisted method of predicting a protein structure, wherein the method employs a database which contains environmental information on the side chain of each amino acid residue contained in the amino acid sequence of each reference protein whose three-dimensional structure is known (column 4, lines 7-11), wherein amino acid

sequence of each of the reference sequence protein is divided into two or more segment sequences comprising two or more contiguous amino acid residues ("cluster vector" column 4, lines 1-6) based on the characteristics of the three-dimensional structure (column 8, lines 27-31) of the reference protein – hydrophilic, hydrophobic (column 3, lines 45-49) – exposed, buried, and partially buried (column 4, lines 15-16), wherein the method comprises the steps of:

a) conducting matching based on the environmental information on each amino acid residue of each of the two or more core segment sequences of the reference protein and hydrophobicity or hydrophilicity property of the side chain of each amino acid residue of the query sequence (column 3, lines 36-49; 37-67; column 4, lines 7-11); and

b) choosing at least one template protein that has the highest similarity (or "best fit score" as described in column 4, lines 27-29; Figure 1, step 140; column 12, lines 63-64), thereby anticipating claims 1, 8, and 10.

With regard to claim 3, Cohen et al. disclose the usage of "cluster vector," step, wherein the process is based on the fact that each residue variability type represents a cluster of residue types at each position of aligned sets of homologous protein sequences (reference proteins with known structures (column 4, line 11)), wherein the cluster characterization is based on the realization that a recurring pattern of variation exists in single positions ***and in short segments of contiguous positions in aligned sets of homologous sequences***" (column 3, lines 57-67).

The target sequence is then mapped into a sequence of residue variability types, ***either based on solubility variability or residue positional variability (or clusters), wherein the sequence is then compared with one or more environmental strings, each of which represents a known protein structure***. (column 4, lines 6-11)

With regard to claim 4, Cohen et al. discuss that the target sequence is compared with one or more environmental strings, each of which represents a known protein structure, wherein the environment string characterizes a known protein structure with respect to the degree of surface exposure of each amino acid in the protein's structure – exposed, buried, and partially buried (or degree of burial) (column 4, line 9-16).

With regard to claims 5-7, drawn to the step of "matching," based on the limitation of, "sliding two ore more core segment sequences of the reference protein on the query sequence with or without consideration of gaps (i.e., insertions or deletions), gaps at one end or both ends of the core segments, the procedure of "scoring matrix" (column 8, line 38), which is disclosed as being generated from a select set of unique three-dimensional protein structures, their associated primary residue sequence and homologous sequences, and their three-dimensional atomic coordinates (column 8, lines 39-41) as well as global alignment which accounts for insertions and deletion (column 12, line 67 to column 13, line 2). As the homologous sequences identified by this process would return protein sequence (or reference sequences) which have gaps such as deletions or insertion indiscriminate with respect to where such gaps would occur, such limitation would clearly be met by the scoring matrix step of Cohen et al.

With regard to claim 9, Cohen et al. disclose the running the query protein against the reference proteins, once based on solubility residue variability measure (column 15, lines 35-37); and next based on cluster residue variability measure, thus involving scores generated from the same proteins, or "self matching." While page 22 of the instant specification discloses an example of the process governing self matching process, there is not a specific definition, and thus, the term was given its broadest reasonable interpretation.

According to MPEP 2106(II)(C), claims are to be given their broadest reasonable interpretation:

> "Office personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. In re Morris, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). ***Limitations appearing in the specification but not recited in the claim are not read into the claim.*** > E-Pass Techs., Inc. v. 3Com Corp., 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" without importing limitations from the specification into the claims unnecessarily).< In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969). See also In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) ("During patent examination the pending claims must be interpreted as broadly as their terms reasonably allow.... The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed.... An ***essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous***. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.").

Additionally, MPEP 2106(II)(C) states that while it is appropriate to use the specification to determine what applicant intends a term to mean, a positive limitation from the specification cannot be read into a claim that does not impose that limitation.

Therefore, the invention as claimed is anticipated by Cohen et al.

### *Conclusion*

No claims are allowed.

### *Inquiries*

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m. The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot

guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Patent Examiner
Art Unit 1637
6/8/2005

YOUNG J. KIM
PATENT EXAMINER

yjk